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ASSOCIATION BETWEEN CRP, D-DIMER, SERUM FERRITIN, INITIAL CT-CHEST SEVERITY SCORE AND THE OUTCOME OF COVID-19 IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Introduction: The surge of Covid -19 pandemic and the earlier depletion of resources have led to the need of allocation of patients based on levels of risk. The COVID 19 related mortality has been on increase in people with old age, male gender, inflammatory markers elevation and in people with history of co morbidities. With this background, thus study aimed to observe association between CRP, D-Dimer, Serum Ferritin, The Initial CT Chest Severity Score and the outcome of Covid 19 in patients with Type 2 Diabetes mellitus. **Materials and methods:** A hospital based retrospective study was done among COVID 19 patients from the period of September to December 2020. Patients with Type 2 diabetes mellitus admitted with RT-PCR positive (or) CT Thorax – CORADS 4 and above with age more than 18 years and having CRP, D-Dimer, Serum Ferritin results within 24 hours after admission were included in the study. The data was collected using a semi structured questionnaire. **Results:** A total of 531 individuals were participated in the study. The mean respiratory rate and oxygen saturation between the survived and deceased groups was statistically significant (p value 0.024 and 0.044 respectively). All the patients had normal blood urea and serum creatinine values. The mean CORADS score of the participants is 4.78 ± 0.60. **Conclusion:** There is statistically significant difference in the mean respiratory rate and mean SPO2 between deceased and recovered patients. With advancements in medical sciences, it may not be a rigid process to predict severity with laboratory investigations.

KEYWORDS : COVID-19, CRP, D-Dimer, CT-Severity score, Mortality, and Salem.

INTRODUCTION:

Coronaviruses, which are enveloped RNA viruses, have its place in the subfamily of Orthocoronavirinae. They widely cause infections in humans and cause zoonotic infections as well. Variants of coronaviruses such as SARS-CoV and MERS-CoV have caused epidemics in 2003 and 2012 respectively.[1] As of October 2021, there were 21.9 crores cases of COVID 19 and 45.5 lakh deaths. In India, there were 3.39 crores cases and 4.49 lakh deaths.[2] The surge of Covid -19 pandemic and the earlier depletion of resources have led to the need of allocation of patients based on levels of risk. For the allocation, specific and more reliable biomarkers are needed that will help to classify the patients based on risk.[3] The disease have a variable clinical course ranging from asymptomatic infections to symptoms such as fever,cough,breathlessness etc.[4] Though RT-PCR sensitivity remains high in diagnosing COVID 19,the delay in results has led the clinicians to go for CT Chest which illustrates the pulmonary involvement.CORADS (Covid 19 reporting and data system).It ranges from very low (CORADS 1) to very high (CORADS 6).[5] Some hospitalised patients may have poor prognosis and progresses for severe viral pneumonia.[4] Cytokine storm has been attributed to be responsible for the complications that occur during COVID 19.The usual complications which is found with COVID 19 include ARDS (Acute respiratory distress syndrome),Acute respiratory failure, Sepsis, Acute liver and kidney injury,DIC (Disseminated Intravascular Coagulation) and Pulmonary embolism.[6] The common investigations routinely done to assess the disease progression in patients include decreased leucocyte count, increased D-Dimer , Serum ferritin,CRP (C-Reactive protein) values and enzyme markers such as creatine kinase. It has been reported that older age and increased values of D-Dimer have been considered the risk factors for mortality in COVID 19 patients.[4] D-Dimer originates from the cross linked fibrin formation and lysis and it reveals the process of blood coagulation and activation of fibrinolysis.[7] COVID 19 related mortality has been on increase in people with old age, male gender, inflammatory markers elevation and in people with history of co morbidities. When persons with co morbidities are infected with COVID 19, immune dysregulation has been discovered to be a factor in increased mortality.[8] With this background, thus study aimed to observe association between CRP,D-Dimer, Serum Ferritin, The Initial CT Chest Severity Score and the outcome of Covid 19 in patients with Type 2 Diabetes mellitus.

MATERIALS AND METHODS:

This is a hospital based retrospective analytical study done among COVID 19 patients admitted to Vinayaka missions' medical college and hospital, Salem. The study period was from September 1st 2020 to 15th December 2020. Being a retrospective analytical study, informed consent was not required. All the patients were retrospectively analysed consecutively. Laboratory tests included complete blood count, blood urea, serum creatinine, C Reactive protein (CRP), D Dimer and Serum Ferritin. Radiological assessment included CT (Computed tomography) of the chest. Patients with Type 2 diabetes mellitus admitted with RT-PCR positive (or) CT Thorax – CORADS 4 and above with age more than 18 years and having CRP, D-Dimer, Serum Ferritin results within 24 hours after admission were included in the study. And those with the history of elevated CRP, D-Dimer, Serum ferritin were excluded from the study. The data was collected using a semi structured questionnaire which consists of presenting complaints of the patient. Complaints were asked for presence (or) absence of fever,cough,loss of breathlessness, loss of smell and taste , loose stools , history of any illness (diabetes,hypertension,CAD,Thyroid

etc,others), general and systemic examination,RT PCR details, findings of CT Chest and other investigations. Finally, survival of the patient was also looked upon. The statistical analysis was performed using SPSS VERSION 20. Categorical variables were expressed as frequencies and percentages. Chi square test, Fischer exact test was used to determine statistical association for variables between the groups. Continuous variables was expressed as mean and standard deviation and the association between the continuous variables is expressed using the Independent t test. Statistically significant association is considered to exist when p value is less than 0.05.(p value < 0.05)

RESULTS:

A total of 531 participants was admitted for COVID 19 in Vinayaka Missions during September 1st to December 15th, 2020.Of the total 531 participants, 23 (4.3%) patients failed to survive. majority of them were in the age group 45 – 59 years (36.9%). Median age was 54 years (interquartile range (IQR) 44 – 63). Majority of the participants were males, who constituted about 72.7%. The socio demographic and baseline characteristics of the study participants among the survived and deceased has been described in table 1. The study subjects were asked for presence (or) absence of symptoms of fever, cough, breathlessness, loss of smell and taste, headache, throat pain and loose stools. The distribution of symptoms has been illustrated in figure 1. When enquired about the co morbid conditions, type 2 diabetes mellitus was present in 31.9% of participants, hypertension was present in 18.8% of the participants, history of coronary artery disease was present in 2.8% of the participants, hypothyroidism was present in 2.1% of the patients and 1.7% of the patients had other co morbidities like epilepsy, acute kidney injury, autoimmune haemolytic anaemia and bronchial asthma. The mean pulse rate of 531 participants was 96.65 ± 15.22 and the difference in the mean pulse rate between the survived and deceased groups was not statistically significant. The mean respiratory rate and oxygen saturation between the survived and deceased groups was statistically significant (p value 0.024 and 0.044 respectively). This has been mentioned in table 2. All the patients had normal blood urea and serum creatinine values. The mean CORADS score of the participants is 4.78 ± 0.60. The distribution of CORADS scoring in CT Chest has been given in figure 2. The difference between the mean of neutrophils, lymphocytes, serum creatinine, blood urea, CRP, D-Dimer and Serum ferritin among the survived and deceased groups was statistically significant

DISCUSSION:

In a study done by Hodges et al[4] among 1310 participants, it was found that 73.1% of the participants survived. The values of CRP, D Dimer, Ferritin and urea was higher in the survived group but except for ferritin, the difference between the groups was statistically significant for other components. In a study done by Ponti et al[3], it was been found that CRP values was elevated in initial phases of infection and it remains the early predictor and increased D Dimer may lead to severe complications and death. In a study done by Huang et al,[9] it was found that elevated CRP of ≥ 10 mg/L has 51% sensitivity and 88% specificity in predicting severity. In a study done by Ullah et al,[10] the odds for in hospital mortality was significantly higher for patients with high CRP and D Dimer. In a meta-analysis done by Henry et al,[11] it was found that patients with severity of disease had increased leucocyte count whereas lymphocyte and platelet counts was decreased and serum ferritin was a strong marker for severe disease. In a review done by Mehraeen et al[12] it was found that mortality in infectious diseases is more common among elderly. This was further supported by studies by Opal et al [13] and Jin et al,[14] in which it was found that elderly age group and male gender has been found to be associated with increased mortality. In a study done by Baay et al,[15] fever was the most common symptom. Among the enzymes, LDH, Troponin, Creatinine and Albumin, LDH has been found to be major predictor of mortality.[16] In a study done by Chilimuri et al,[17] it was found that out of 375 patients, 57% survived and odds of increasing mortality and statistically significant association between the groups was found with D-Dimer values more than 1000 ng/Ml and CRP values more than 200 mg/L. In a meta-analysis done by Kermali et al,[18] it was found that increased levels of CRP, D-Dimer, ferritin, urea and creatinine was found to be closely related to COVID 19. It was also found that high WBC count and neutrophil count also predicts severity. A study done by Qin et al,[19] shows that Neutrophil lymphocyte ratio is significantly higher in severe COVID 19 patients. In a study done by Chen et al,[20] it was found that raised serum creatinine levels is associated with poor outcome in COVID 19. Binding of COVID 19 virus to ACE2 (Angiotensin converting enzyme – 2) inhibitors in vascular endothelial cells leads to endothelial dysfunction, the function of which has been already decreased by pre-existing morbidity due to cardiovascular diseases and hypertension. Impaired T cell response in diabetics has also been attributed to increased mortality.Upregulation of ACE2 receptors by use of medications like ACE (Angiotensin converting enzyme) inhibitors and angiotensin receptor blockers have been found to facilitate the entry of coronavirus into pneumocytes.This has been found to increase the severity of infection.[12]

Table 1: Socio-demographic characteristics and baseline characteristics of the study participants

S. no	Characteristics	Total (n=531)	Survived (n=508)	Deceased (n=23)	P value
1)	Age in years	53.29 ± 14.31	53.36 ± 14.26	51.87 ± 15.55	0.626
2)	Gender				
	Male	386(72.7%)	374 (73.6%)	12(52.2%)	0.154**
	Female	145(27.3%)	134 (26.4%)	11(47.8%)	
3)	Presence of Symptoms				
	Fever	223(42%)	212(41.7%)	11(47.8%)	0.562*
	Cough	160(30.1%)	151(29.7%)	9(39.1%)	0.336*
	Breathlessness	160(30.1%)	150(29.5%)	10(43.5%)	0.154
	Loss of smell and taste	191(36%)	183(36%)	8(34.8%)	0.903
	Headache	187(35.2%)	180(35.4%)	7(30.4%)	0.624
	Throat pain	110(20.7%)	106(20.9%)	4(17.4%)	0.688**
	Loose stools	118(22.2%)	111(21.9%)	7(30.4%)	0.333*

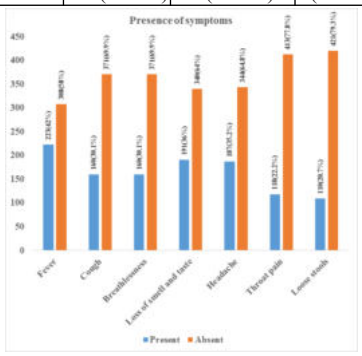

Figure 1: Symptoms of the study participants

Table 2: Presence of comorbidities and distribution of vitals among Survived and Deceased Group

1)	Presence of comorbidities				P - Value
	Type 2 Diabetes Mellitus	169 (31.9%)	164 (32.3%)	8(21.7 %)	0.052
	Systemic hypertension	100 (18.8%)	94(18.5%)	6(26.1 %)	0.363**
	Coronary artery disease	15(2.8%)	14 (2.8%)	1(4.3%)	0.652**
	Thyroid disorders	11(2.1%)	11(2.2%)	-	0.476**
	Others	9(1.7%)	8(1.6%)	1(4.3%)	< 0.05**
2)	Pulse rate	96.65 ± 15.22	96.63 ± 15.3	97.22 ± 12.3	0.856** *
3)	Respiratory rate	21.05 ± 4.78	20.95 ± 4.65	23.26 ± 6.85	0.024** *
4)	O2 Saturation	94.17 ± 5.31	94.96 ± 4.34	93.09 ± 4.78	0.044** *

*- Chi square test
** - Fischer exact test
*** - Independent T test

Table 3: Imaging and laboratory investigations among the survived and deceased participants

1)	RT PCR				
	Positive	437(82.3%)	417 (82.1%)	20(87%)	0.550**
	Negative	94(17.7%)	91(17.9%)	3(13%)	
2)	HRCT CORADS SCORE	4.78 ± 0.60	4.77 ± 0.60	4.91 ± 0.59	0.273***

3)	Hemoglobin	13.59 ± 0.93	13.59 ± 0.92	13.53 ± 1.09	0.761***
4)	Neutrophil (in percentage)	75.3 ± 11.20	72.04 ± 11.88	78 ± 12.33	0.01***
5)	Lymphocyte(in percentage)	22.18 ± 9.4	24.16 ± 8.43	20.04 ± 10.46	0.02***
6)	Serum creatinine	0.86 ± 0.10	0.83 ± 0.10	0.89 ± 0.20	< 0.05***
7)	Blood urea	16.76 ± 1.56	16.40 ± 0.96	17.13 ± 2.16	0.001***
8)	CRP	2314 ± 124.76	584 ± 33.15	4044 ± 216.37	<0.001***
9)	D Dimer	12669 ± 1232.52	12368 ± 1178.02	12980 ± 2436.22	0.02***
10)	Serum ferritin	1040 ± 350.30	960 ± 346.78	1120 ± 367.19	0.04***

*- Chi square test
** - Fischer exact test
*** - Independent T test

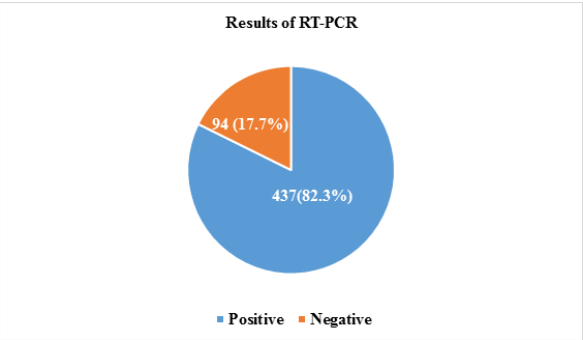

Figure 2: Results of RT-PCR of study participants

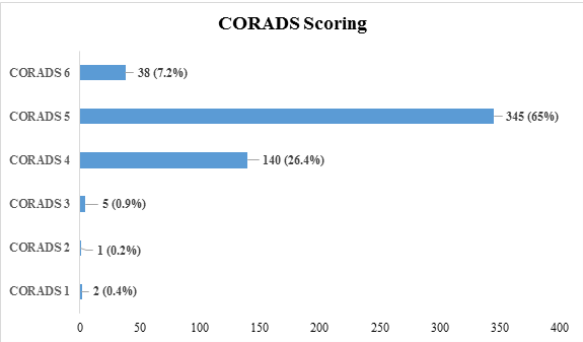

Figure 3: CORADS scoring of the study participants

CONCLUSION:

There is statistically significant difference in the mean respiratory rate and mean SPO2 between deceased and recovered patients. With advancements in medical sciences, it may not be a rigid process to predict severity with laboratory investigations. By doing so, it can be used as a base for treatment and for prediction of mortality among COVID 19 patients. Thus, early diagnosis and appropriate treatment remain the main line of prevention in this disease. By means of increased mortality in older age people and people with co morbidities, it is better to prioritise them for effective management.

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CONFLICT OF INTERESTS: There is no conflict of Interest

AUTHORS CONTRIBUTION: All authors in this study contributed to the data collection of the patients

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